Annals of Clinical and Analytical Medicine
Original Research

Evaluation of sleep quality in rheumatoid arthritis patients

Rheumatoid arthritis' therapy impact on sleep

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Abstract

Aim: The purpose of this study was to evaluate treatment effects on sleep quality and fatigue in patients with RA. Besides, we aim to examine possible effects of disease activity, pain and socio-demographic features on sleep quality and fatigue.

Material and Methods: In this study, 78 patients diagnosed with RA according to the American Rheumatism Association (ACR) 1987 revised criteria and European League Against Rheumatism (EULAR) criteria were compared with a parallel healthy control group (n=48). All participants were given a socio-demographic questionnaire, the Pittsburgh Sleep Quality Index (PSQI), Multidimensional Assessment of Fatigue Scale (MAF), Visual Analog Scale (VAS), Disease Activity Score 28 (DAS28).

Results: The mean duration of diagnosis was 9.10±8.54 years and the mean score of DAS28 was 3.25±1.04 in patients with RA. In terms of total PSQI, the differences between two groups were found statistically significant (p=0.001; t=8.023). In terms of MAF, The differences between two groups were found statistically significant (p=0.001; t=3.668). The sleep disturbance and daytime functioning scores were found as 1.86 ± 0.69, 1.40 ± 0.83 respectively in non-biological DMARD group and 1.54±0.66; 0.84±0.93 in biological + non-biological DMARD group. There were statistically significant differences between groups (p=0.043; t=2.054, p=0.008; t=2.730). According to correlation analysis between DAS28 and disease duration, a positive correlation has been found (r = 0.297; p = 0.008).

Discussion: Patients with RA generally experience more fatigue and have worse sleep quality than healthy individuals. High disease activity can lead to longer sleep latency, reduced daytime functionality, and increased fatigue symptoms.

Keywords

Rheumatoid Arthritis, Pittsburgh Sleep Quality Index, Multidimensional Assessment of Fatigue Scale, Visual Analog Scale, Disease Activity Score-28

DOI: 10.4328/ACAM.22050 Received: 2023-11-15 Accepted: 2024-01-01 Published Online: 2024-03-27 Printed: 2024-05-01 Ann Clin Anal Med 2024;15(5):307-312
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This study was approved by the Ethics Committee of Cumhuriyet University (Date: 2013-02-12, No: 2013-02/11)

Introduction

Rheumatoid arthritis (RA) is a long-term autoimmune condition that causes inflammation, resulting in swollen joints and joint pain [1]. The chronic process of rheumatoid arthritis negatively affects physical, psychological, emotional and social functions from early stage of disease. Moreover, it causes deterioration of life quality among individuals [2]. The current treatment options can neither prevent RA nor treat completely. Therefore, the main purpose in treatment of RA is to minimize negative impact of disease on life by increasing life quality and decreasing disability. For an effective treatment protocol, the relationships between RA, functional status and quality of life must be well established. [3].

Sleep is one of the factors that affect life quality in patients with RA. Insufficient sleep is associated with impaired life quality, increased pain perception and morbidity/mortality in patients [2, 3]. The frequency of sleep disturbance problem ranges from %54 to %70 in patients with RA [4]. Therefore, accurate evaluation of sleep quality in RA has become more important recently [2]. It was observed that sleep fragmentation has caused more problems than sleep stage changes in patients with RA. Thus RA patients have longer duration of sleep latency, they wake up several times during the night, wake up early in the morning and have excessive daytime sleepiness [3, 4]. Although the sleep quality and fatigue have been examined in numerous researches, there are limited published data related to treatment impact on sleep quality and fatigue. Similarly there are also limited published data related to agents used in the treatment and their effects on sleep quality and fatigue [5]. The purpose of this study was to evaluate treatment effects on sleep quality and fatigue in patients with RA. In addition, we aim to examine possible effects of disease activity, pain and socio-demographic features on sleep quality and fatigue.

Material and Methods

The study was conducted at the Department of Physical Medicine and Rehabilitation, Cumhuriyet University, Faculty of Medicine, from March to December 2013. In this study, 78 patients diagnosed with RA according to the American Rheumatism Association (ACR) 1987 revised criteria and European League Against Rheumatism (EULAR) criteria were compared with a parallel healthy control group (n=48). All participants were enrolled in this study after obtaining written informed consent. Exclusion criteria for this study were accompanying psychiatric disorders, administration of psychotropic drugs which may effect on sleep, mental retardation and presence of a chronic systemic disease except RA.

Socio-demographic Questionnaire

This questionnaire includes socio-demographic data such as age, gender, educational state, socio-economical level and marital status of patients and control group.

Pittsburgh Sleep Quality Index (PSQI)

The PSQI is a tool used by patients to self-evaluate their sleep quality. It looks at seven different aspects of sleep, including the individual's perception of their sleep quality, the time it takes to fall asleep, the duration of sleep, the efficiency of sleep, any disturbances during sleep, the use of sleep medication, and any dysfunction during the day. It also provides a total score for overall sleep quality. Validity and Reliability were performed by Agargün et al. in our country [6].

Multidimensional Assessment of Fatigue Scale (MAF)

The MAF inventory, developed by Belza et all., evaluates fatigue assessment in terms of five dimensions. The dimensions are labeled fatigue severity, frequency, daily function and psychological status. Each items' outcome scores range from 0 to 10 and maximum score is determined as 50 points. It was explained to patients that higher scores indicates severe fatigue (0= no fatigue, 10= severe fatigue) [7].

Visual Analog Scale (VAS)

The VAS was used to measure of instant pain intensity in patients. The pain scale ratings range from 0 (no pain) to 10 (intolerably severe pain) [8].

Disease Activity Score 28 (DAS28)

The DAS28 was used to evaluate disease activity. Disease Activity Score calculated with the formula [0.56×The number of tender joints (TJ28) + 0.28×The number of swollen joint (SJ28) + 0.014× General Health Assessment (GHA) + 0.70× Erythrocyte Sedimentation Rate (ESR)]. The special type calculator is available to use these calculations. In the obtained results, level of disease activity has been accepted as low (DAS28 ≤ 3.2) and high (DAS28 > 3.2). [9].

Statistical Analysis

SPSS (Statistical Package for the Social Sciences, USA) software was used for analysis of data. Data were expressed as mean, standard deviation and percentage. The initial evaluation and comparison of normally distributed data were done using the Kolmogorov-Smirnov test. The Chi-square test was used for comparisons between multiple groups. The Pearson tests were used to analyze the presence of correlation. Statistical significance was determined by a p value of less than 0.05.

Ethical Approval

This study was approved by clinical ethics committee of Cumhuriyet University (Date: 2013-02-12, No: 2013-02/11).

Results

The research encompassed 78 individuals with RA and a control group of 48 healthy individuals. The average age of the participants in the patient group was found to be 48.08±10.95, while it was 45.70±6.98 in the control group. There were no significant disparities in terms of average age and gender between the patient group and the control group. The patient group in this study consisted of 11 males (14.1%) and 67 females (85.9%), while the control group comprised 11 males (22.9%) and 37 females (77.1%). The average duration of diagnosis for the patients with RA was 9.10±8.54 years, and the average DAS28 score was 3.25±1.04.

The mean of total PSQI in patient group was found to be 8.46±3.9, in control group was 4.04±2.24. There was a statistically significant differences between groups according to total PSQI means (p=0.001; t=8.023). The total mean score of MAF was 28.25±13.43 in the patient group and in the control group was 20.16±11.05. The differences between two groups were found statistically significant (p=0.001; t=3.668). The mean scores of all sub-scales of PSQI were statistically significant among the patient and control groups (Table 1).

Individuals' sleep quality in this study was evaluated as 'good sleep quality' (PSQI ≤ 5) and 'poor sleep quality' (PSQI > 5) according to total PSQI score. When evaluated according to whether it is a good or poor sleep quality, statistically significant differences were found between the groups

Table 1. The comparison between Pittsburgh sleep quality index scores and total score of MAF fatigue scale of patient and control groups. *: Student's t-test. Std: Standard deviation, MAF: Multidimensional Assessment of Fatigue Scale, PSQI: Pittsburgh Sleep Quality Index

Pittsburgh Sleep Quality Index	Group	Mean ± Std. Deviation	p value	t value
Subjective sleep quality	Patient	1.35±0.77	0.001*	3.921
	Control	0.93±0.43		
Sleep latency	Patient	1.83±1.03	0.001*	6.237
	Control	0.81±0.781		
Sleep duration	Patient	1.10±1.16	0.001*	4.164
	Control	0.39±0.73		
Habitual sleep efficiency	Patient	1.26±1.13	0.001*	7.221
	Control	0.18±0.53		
Sleep disturbances	Patient	1.73±0.69	0.001*	4.575
	Control	1.16±0.63		
Daytime Functionality	Patient	1.16±0.91	0.001*	4.027
	Control	0.54±0.71		
Total PSQI	Patient	8.46±3.9	0.001*	8.023
	Control	4.04±2.24		
MAF	Patient	28.25±13.43	0.001*	3.668
	Control	20.16±11.05		

Student's t-test. Std: Standard deviation, MAF: Multidimensional Assessment of Fatigue Scale, PSQI: Pittsburgh Sleep Quality Index.

Table 3. The correlation between disease duration, sleep subcomponents, fatigue, pain and disease activity in RA patients. *: Low correlation, **: High correlation, Std: Standard deviation. DAS28: Disease Activity Scale 28, MAF: Multidimensional Assessment of Fatigue Scale, PSQI Pittsburgh Sleep Quality Index, RA: Rheumatoid Arthritis, VAS: Visual Analog Scale

Parameters	MAF	VAS	DAS28	Disease Duration
MAF		r = 0.562**	r = 0.394**	r = 0.188
		p= 0.001	p= 0.001	p= 0.099
VAS	r = 0.562**			r = 0.181
	p= 0.001			p= 0.113
DAS28	r = 0.394**			r = 0.297**
	p: 0.001			p= 0.008
Total PSQI	r =0.550**	r = 0.476**	r = 0.218	r = 0.074
	p= 0.001	p= 0.001	p= 0.056	p= 0.519
Subjective Sleep Quality	r =0.430**	r = 0.238*	r = 0.018	r = 0.114
	p= 0.001	p= 0.036	p= 0.875	p= 0.321
Sleep Latency	r =0.296**	r = 0.381**	r = 0.251*	r = 0.020
	p= 0.009	p= 0.001	p= 0.027	p= 0.861
Sleep Duration	r = 0.314**	r = 0.276*	r = 0.105	r = 0.082
	p= 0.005	p= 0.014	p= 0.361	p= 0.476
Habitual Sleep Efficiency	r = 0.351**	r = 0.242*	r = 0.052	r = 0.054
	p= 0.002	p= 0.033	p= 0.653	p= 0.640
Sleep Disturbances	r = 0.415**	r = 0.414**	r = 0.151	r = 0.008
	p= 0.001	p= 0.001	p= 0.188	p= 0.943
Daytime Functionality	r = 0.511**	r = 0.442**	r = 0.321**	r = 0.021
	p= 0.001	p= 0.001	p= 0.004	p= 0.852

*: Low correlation, **: High correlation, Std: Standard deviation. DAS28: Disease Activity Scale 28, MAF: Multidimensional Assessment of Fatigue Scale, PSQI Pittsburgh Sleep Quality Index, RA: Rheumatoid Arthritis, VAS: Visual Analog Scale.

Table 2. Pittsburgh index scale scores, fatigue, pain and disease activity relationships according to treatment of patients. Std: Standard deviation. DAS28: Disease Activity Score 28, DMARD: disease modifying anti-rheumatic drug, MAF: Multidimensional Assessment of Fatigue Scale, PSQI: Pittsburgh Sleep Quality Index, RA: Rheumatoid Arthritis, VAS: Visual Analog Scale

Significances according to treatments	Group	Mean ± Std. Deviation	p value	t value
Subjective Sleep quality	Non-biological DMARD	1.37±0.74	0.804	0.250
	Non-biological DMARD and biological DMARD	1.33±0.81		
Sleep Latency	Non-biological DMARD	1.91±1.04	0.443	0.771
	Non-biological DMARD and biological DMARD	1.72±1.03		
Sleep Duration	Non-biological DMARD	1.24±1.22	0.213	1.257
	Non-biological DMARD and biological DMARD	0.90±1.07		
Habitual Sleep Efficiency	Non-biological DMARD	1.28±1.12	0.860	0.177
	Non-biological DMARD and biological DMARD	1.24±1.17		
Sleep Disturbances	Non-biological DMARD	1.86±0.69	0.043	2.054
	Non-biological DMARD and biological DMARD	1.54±0.66		
Daytime Functionality	Non-biological DMARD	1.40±0.83	0.008	2.730
	Non-biological DMARD and biological DMARD	0.84±0.93		
Total PSQI	Non-biological DMARD	9.08±3.87	0.100	1.665
	Non-biological DMARD and biological DMARD	7.60±3.89		
MAF	Non-biological DMARD	30.94±13.91	0.038	2.109
	Non-biological DMARD and biological DMARD	24.59±12.01		
VAS	Non-biological DMARD	3.71±2.37	0.462	0.740
	Non-biological DMARD and biological DMARD	3.30±2.45		
DAS28	Non-biological DMARD	3.29±0.95	0.722	0.358
	Non-biological DMARD and biological DMARD	3.20±1.16		

Std: Standard deviation. DAS28: Disease Activity Score 28, DMARD: disease modifying anti-rheumatic drug, MAF: Multidimensional Assessment of Fatigue Scale, PSQI: Pittsburgh Sleep Quality Index, RA: Rheumatoid Arthritis, VAS: Visual Analog Scale.

(x2=39.763; p=0.001); In the patient group, 17 of 78 patients (21.8%) had good sleep quality, and 61 (79.2%) patients had poor sleep quality. In the control group, 38 of 48 patients (79.2%) had good sleep quality and 10 (20.8%) had poor sleep quality. Patients were dichotomized as good and bad sleepers, and then compared according to DAS 28. Participants were classified according to DAS28 score as inactive or low disease activity patients (DAS28 score ≤3.2) and active or high disease activity patients (DAS28 score> 3.2). The disease was inactive in 12 (70.6%) of 17 good sleeper patients, active in 5 (29.4%) patients. In addition, disease was inactive in 31 (50.8%) of 61 bad sleeper patients, active in 30 (49.2%) patients. However, the rate of high disease activity in bad sleeper patients was higher than good sleeper patients, and there were no significant differences found between groups (x2=2.100; p=0.147).

The total PSQI score was found as 7.74±3.86 in low disease activity patients and 9.34±3.88 in high disease activity patients. There were no significant differences between the groups (p=0.074; t=1.813). The sleep latency and average of daytime functioning score was found as 1.53±1.00, 0.88±0.82 respectively in low disease activity patients and 2.20±0.96, 1.51±0.91 respectively in high disease activity patients. The difference between the two group was statistically significant (p=0.004; t=2.955, p=0.002; t=3.194 respectively). There was no statistically significant difference observed between the groups in other sleep quality sub-scales. Besides, the mean of MAF score was detected as 23.81±12.79 in low disease activity patients and 20.16±11.05 in high disease activity patients (p=0.001; t=3.459).

The patients were divided into two groups according to treatment. The first group received non-biologic DMARD treatment (n=45), while the second group was treated with a combination of non-biological and biological DMARD (n=33). According to examination results of all Pittsburgh sleep quality parameters, total PSQI score of non-biological DMARD group was found 9:08 ± 3.87. As for the biological + non-biological DMARD group, it was 7.60 ± 3.89. The difference was not statistically significant although lower total PSQI score was obtained from biologically + non-biological group (p=0.100; t=1.665). In the group treated with non-biological DMARDs, the scores for sleep disturbance and daytime functioning were found to be 1.86 ± 0.69 and 1.40 ± 0.83 respectively. In the group treated with both biological and non-biological DMARDs, these scores were 1.54±0.66 and 0.84±0.93 respectively. Statistically significant differences were observed between the groups (p=0.043; t=2.054, p=0.008; t=2.730). The MAF score was also different between the groups, with a score of 30.94±13.91 in the non-biological DMARD group and 24.59±12.01 in the group treated with both biological and non-biological DMARDs, indicating a statistically significant difference (p=0.038; t=2.109) (Table 2).

In terms of all PSQI sub-scales, MAF, VAS and DAS28 values There were no statistically significant differences between anti-TNF treated patients (n=20) and non-TNF treated patients (n=13). In our study, according to correlation analysis between DAS28 and disease duration, a positive correlation was found (r = 0.297; p = 0.008). Positive correlation was observed in all components of sleep quality and disease activity in correlation table (Table 3). There was statistically significant difference between the groups according to MAF scores (p=0.001; t=6.438). The average MAF score in individuals who had good and poor sleep quality was found as 17.87±10, 30.83±12.43 respectively.

Discussion

In present study, effects of treatment on various components of fatigue and sleep quality were examined in RA patients. Total PSQI and also all subgroups of PSQI were found worse in RA patients than healthy controls. When comparing treatment in patients, PSQI sleep disturbance and daytime functionality parameters performed better in patients treated with combination of non-biological and biological DMARD than non-biological DMARD therapy only. Besides, the fatigue scores were found lower in patients who were treated with combination of non-biological and biological DMARD therapy.

A considerable amount of RA patients stated that this disease prevent their sleep with co-occurrence of fatigue [2]. Difficulties in falling asleep, poor sleep quality and restfulness sleep were observed as well. The PSQI, or Pittsburgh Sleep Quality Index, is a tool that individuals can use to self-evaluate their sleep quality and duration. It was originally developed to analyze sleep patterns over a period of one month [10, 11]. Recently sleep quality of RA patients were examined with PSQI inventory [10, 11]. The RA patients had significantly worse sleep quality than healthy control groups according to total PSQI in those published data [10, 11]. Despite few studies with PSQI; influencing factors on sleep quality have not been examined well therefore etiology of sleep remains unclear in RA patients. Ulus et al. evaluated fatigue with MAF inventory in their sleep assessment research with PSQI. MAF scale is found to be useful in RA patients [12]. In this study, the fatigue score was found higher in RA patients than control group. Numerous researches have reported that the fatigue has impact on the subjective sleep quality and total PSQI score in RA patients with poor sleep [10, 11]. Impaired sleep quality and increased fatigue results obtained from our study in RA patients were found to be consistent with related published data. Additionally a positive correlation was found between MAF score and all sub-component of PSQI scale in our study.

Recently, Westhovens et al. [13] found a positive correlation between DAS28 and C-reactive protein levels with PSQI scores, while a negative correlation was observed with the Epworth Sleep Scale in relation to the disease activity of RA patients. A significant body of research has indicated that disease activity is a key factor influencing sleep quality. Furthermore, it has been observed that disease activity can have varying impacts on the seven sub-components of the PSQI [14]. Nicassio et al [14] have reported that DAS28 have no effect on PSQI. Fragia et al. [15] did not find any correlation between decreasing of disease activity and sleep disorders after the tocilizumab treatment. Results of our study showed that disease activity did not significantly affect the total PSQI score. It was affected only sleep latency and daytime functioning parameters. The differences in clinical characteristics of patients or study and patients' subjective reasons may influence results.

Cytokines and immune functions, which have a regulation effect on sleeping-waking in brain and behavior, could

influence the function and activation of patients with arthritis [16]. Specifically, TNF and IL-1 are not only provided biological activation of inflammatory disease but also provide homeostatic regulation in sleep/wake states. Symptoms such as sleep loss, sleepiness, fatigue, poor cognition and enhanced sensitivity to pain may be seen due to injection of exogenous IL1 or TNF [16]. Beneficial effects of DMARDs treatment in RA have been observed on pain, energy and sleep [16]. Positive acute changes with infliximab treatment of RA were reported in night sleep physiology and day sleep [16]. Vgontzas et al [17] applied etanercept, another TNF antagonist, in RA patients with obstructive sleep apnea and improvement in sleep latency moreover decreasing of sleepiness has been observed. The significant improvement was reported in pain, fatigue, sleep, physical and mental functions after 2 years of abatacept treatment in patients with an inadequate response to anti-TNF therapy.

Westhovens et al [13] were reported that sleep quality impaired in patients with uncontrolled treatment. Fatigue scores were decreased in patients with adalimumab treatment in long-term studies. However it was not statistically significant Solak et al [18] found that PSQI and pain scores were numerically lower in RA patients treated with anti-TNF agents. Taylor et al [19] could not detect any differences between Epworth sleepiness scale or PSQI scores, despite improvement in subjective fatigue after anti-TNF therapy and sleep efficiency in polysomnography. In study of Wolfe et al [20] RA patients were compared with FMF and individuals who had not any inflammatory diseases and sleep problems did not decrease even anti-TNF agent treatment. Sarıyıldız et al [21] were compared RA patients according to treatment and treatment did not affect the PSQI in analysis of cross-sectional data.

Our analysis did not reveal a notable enhancement in the overall PSQI scores of patients who received a mix of biological and non-biological DMARDs compared to those who were treated with only non-biological DMARDs. This observation aligns with previously reported studies. In recent studies, biological agent therapy was improved quality of sleep, although there was no significant improvement according to total PSQI in our study. The differences of study methods and patients' features may cause these results. In contrast to previous research, no significant variations were observed in the impact on sleep quality and fatigue when patients on biologic agents were split into two categories: anti-TNF and non-anti-TNF.

Limitation

There was a limitation in our study. The assessment of sleep was examined with a self-report instrument without polysomnographic measurements. Additionally we held a cross-sectional examination in our study.

Conclusion

To sum up, patients who were treated with a mix of biological and non-biological DMARDs showed better results in the sleep disturbance and daytime functionality aspects of the PSQI compared to those who only received non-biological DMARDs. Additionally, the combined therapy of biological and non-biological DMARDs was found to have a beneficial effect on patient fatigue.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

Funding: *None*

Conflict of Interest

The authors declare that there is no conflict of interest.

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How to cite this article:
Mehmet Siddik Tuncay, Ozlem Sahin, Murat Semiz, Esra Semiz, Bulent Alim, Halil Peksen, Salih Salihoglu, Muhammed Fatih Sabuncu, Mehmet Salih Kilic, Ali Tavasli. *Evaluation of sleep quality in rheumatoid arthritis patients. Ann Clin Anal Med 2024;15(5):307-312*

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